ACUTE TOXICITY SUMMARY

ETHYLENE GLYCOL MONOETHYL ETHER ACETATE

(2-ethoxyethyl acetate, Cellosolve acetate)

CAS Registry Number: 111-15-9

I. Acute Toxicity Summary (for a 6-hour exposure)

Inhalation reference exposure level	**140 μg/m³**
Critical effect(s)	developmental defects
Hazard Index target(s)	Reproductive/developmental; Nervous System

II. Physical and Chemical Properties (HSDB, 1994 except as noted)

Description	colorless liquid
Molecular formula	$C_6H_{12}O_3$
Molecular weight	132.2
Density	0.975 g/cm^3 @ 20°C
Boiling point	156°C
Melting point	-61.7°C
Vapor pressure	2 mm Hg @ 20°C
Flashpoint	49° C (ACGIH, 1991)
Explosive limits	upper = 12.7% lower = 1.7%
Solubility	soluble in water, alcohol, ether, acetone
Odor threshold	0.060 ppm (geometric mean) (AIHA, 1989)
Odor description	mild, ester-like odor
Metabolites	ethylene glycol monoethyl ether, ethoxyacetic acid (Groesenken *et al*., 1987)
Conversion factor	1 ppm = 5.41 mg/m³ @ 25°C

III. Major Uses or Sources

Ethylene glycol monoethyl ether acetate (EGEEA) is used as a solvent for nitrocellulose, low viscosity cellulose, and resins (Doe, 1984). It is also used as a solvent in coating applications for automobiles, coils, machinery and equipment, and metal furniture and appliances (NIOSH, 1991).

IV. Acute Toxicity to Humans

Headaches, lethargy, sinus problems, nausea, and heartburn were reported by two silk screening workers following occupational exposures ranging from 0.5 to 3.9 ppm (3 to 21 mg/m³) EGEEA (Boiano, 1983). Both workers reported that their symptoms improved when they were away

from work. Dermal absorption and concomitant exposure to other organic solvents may have contributed to the observed symptoms.

It was reported in a human pharmacokinetic study that EGEEA was converted to ethylene glycol ethyl ether (EGEE) by plasma esterases and subsequently metabolized to ethoxyacetic acid (Groeseneken *et al*., 1987). Ethoxyacetic acid, accounting for 22.2% of the absorbed dose, was found in the urine of EGEEA exposed subjects.

Predisposing Conditions for EGEEA Toxicity

Medical: Persons with preexisting eye, respiratory, or neurologic conditions may be more sensitive to the effects of EGEEA exposure (Reprotext, 1999).

Chemical: Persons with concurrent exposure to ethylene glycol monoethyl ether (EGEE) or to ethylene glycol may be more sensitive to the effects of EGEEA exposure because EGEE is a metabolite of EGEEA (Reprotext, 1999).

V. Acute Toxicity to Laboratory Animals

An 8-hour LC_{50} in female rats is reported as 2,200 ppm (12,000 mg/m³) EGEEA (Pozzani *et al*., 1959). However, the lethality data were generated using chemical mixtures, not EGEEA alone.

Hemoglobinuria and hematuria were observed in rabbits following a 4-hour exposure to 2,000 ppm (11,000 mg/m³) EGEEA (Truhaut *et al*., 1979). No other signs of toxicity were noted either during a post-exposure observation period or at necropsy.

Osmotic fragility was compared in the erythrocytes of EGEEA exposed animals and unexposed animals (Carpenter *et al*., 1956). The erythrocytes of rats exposed to 62 ppm (340 mg/m³) EGEEA for 4-hours exhibited increased osmotic fragility as compared to the erythrocytes of unexposed rats. No increase in erythrocyte fragility was observed following a 4-hour exposure to 32 ppm (170 mg/m³) EGEEA.

VI. Reproductive or Developmental Toxicity

EGEEA is listed under California Proposition 65 (Cal/EPA, Safe Drinking Water and Toxic Enforcement Act of 1986) as a reproductive hazard.

Tinston and colleagues (1983) exposed pregnant rabbits to 25, 100, or 400 ppm (140, 500, or 2,000 mg/m³) EGEEA 6 hours per day on days 6-18 of gestation. Significant maternal toxicity, as indicated by decreased food consumption and body weight, and a significant reduction in hemoglobin concentration were observed in the rabbits exposed to 400 ppm EGEEA. One fetus in the 25 ppm EGEEA exposed group had agenesis of the left kidney. Right kidney agenesis was observed in one fetus in the 400 ppm EGEEA exposed group. A review of the data is presented by Doe (1984).

In another study, embryotoxicity was observed following exposure of pregnant rats to 390 and 600 ppm (2,100 and 3,000 mg/m³) EGEEA 7 hours per day on days 7-15 of gestation (Nelson *et al*., 1984). Decreased fetal body weight and a statistically significant increase in the incidence of heart, umbilicus, and rib malformations were observed in rats following maternal exposure to 130 ppm (700 mg/m³) EGEEA. No significant maternal toxicity was noted.

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Mild Adverse Effect Level

Because the most sensitive effect observed is developmental toxicity, a severe adverse effect, and since this effect occurs at or below the threshold for a mild adverse effect, no mild adverse effect level is recommended.

Reference Exposure Level for a 6 hour exposure (protective against severe adverse effects): 140 μg/m³

Because of the uncertainty of extrapolating from a repeated dose study to a one-hour concentration, for the reproductive/developmental endpoint, we have chosen to use one-day's exposure as the basis for the REL. Thus, for EGEEA the REL is for a 6-hour exposure.

Study	Tinston *et al*., 1983
Study population	pregnant rabbits
Exposure method	inhalation of 25, 100, or 400 ppm 6 hours per day on days 6-29 of gestation.
Critical effects	developmental defects
LOAEL	25 ppm
NOAEL	not observed
Exposure duration	6 hours
LOAEL uncertainty factor	10
Interspecies uncertainty factor	10
Intraspecies uncertainty factor	10
Cumulative uncertainty factor	1,000
Reference Exposure Level	0.025 ppm (0.14 mg/m³; 140 μg/m³)

Significantly decreased fetal weights and increased incidence of skeletal defects were observed following exposure to 100 or 400 ppm EGEEA. Maternal toxicity as indicated by a dose-related decrease in food consumption was observed in all exposed groups. Kidney agenesis was observed in one fetus from both the 25 ppm and 400 ppm EGEEA exposure groups. Thus, the LOAEL for developmental effects was 25 ppm.

Level Protective Against Life-threatening Effects

No recommendation is made due to the limitations of the database.

NIOSH (1995) lists a (revised) IDLH of 500 ppm for 2-ethoxyethyl acetate, based on acute inhalation toxicity (specifically lethality) data in animals (Pozzani *et al*., 1959; Smyth *et al*., 1941; Truhaut *et al*., 1979), but states that it may be a conservative value due to the lack of relevant acute inhalation toxicity data for workers.

VIII. References

(ACGIH) American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Cincinnati (OH): ACGIH; 1991. p. 567-568.

(AIHA) American Industrial Hygiene Association. Odor thresholds for chemicals with established occupational health standards. Akron (OH): AIHA; 1989. p. 18.

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(NIOSH) National Institute for Occupational Safety and Health. Criteria for a recommended standard. Occupational exposure to ethylene glycol monomethyl ether, ethylene glycol monoethyl ether, and their acetates. Cincinnati (OH): US Department of Health and Human Services, Public Health Service, Centers for Disease Control, NIOSH, Division of Standards for Development and Technology Transfer; 1991.

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